

Recently, the manufacturer of Diprivan published an article presenting its view on safety of propofol as well as the pathophysiology of propofol infusion syndrome.<sup>7</sup> This report mentions the above-presented trial, but unfortunately lacks further relevant information from this.

This leads to two serious problems. First, without presentation of all data from trial 0859IL-0068, an interpretation of the results from this study and especially the mortality rates is significantly limited. Second, additional studies as proposed by Wysowski and Pollock<sup>1</sup> may be impossible from an ethical point of view.

Therefore, the complete information from trial 0859IL-0068 should be submitted to a peer-reviewed journal to enable presentation of all relevant data and to have the chance to get more insights into the effects and safety of propofol in (pediatric) intensive care medicine.

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**In Reply:**—As stated in our article describing reports of death with propofol for pediatric and adult nonprocedural (long-term) sedation,<sup>1</sup> our analyses of US deaths with propofol, along with case reports, case series, and studies reported in the medical literature, indicate that higher doses, higher concentrations, and usually longer duration of propofol administration were the common factors associated with most cases of propofol infusion syndrome in children and adults. As pointed out by Ahlen *et al.*, the drug's efficacy and safety for sedation of pediatric patients with various disorders (e.g., seizures, head trauma and elevated intracranial pressure, respiratory failure and disorders) have not been established in clinical trials. Because our analysis was descriptive and because we lack studies of these disorders, it is not possible to determine whether they increase the risk of propofol infusion syndrome and death. Intuitively, patients with traumatic head injuries and status epilepticus might be expected to be at increased risk of a poor outcome. However, we note that many patients in our case series and in the published literature were sedated for agitation, respiratory conditions such as croup and stridor, and postsurgery—less serious conditions where death would be unexpected.

The US product labeling for propofol states that Diprivan Injectable

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## Protective Ventilation during One-lung Ventilation

**To the Editor:**—I read with interest the report by Michelet *et al.*<sup>1</sup> For many years, hypoxemia was considered as the most important—if not the only—problem during one-lung ventilation (OLV). Therefore, the guidelines are primarily aimed at preventing and treating the hypoxemia.<sup>2</sup> Since Katz *et al.*<sup>3</sup> found that large tidal volumes produced the highest arterial oxygen tension (Pao<sub>2</sub>) during OLV, one can find in these guidelines that the tidal volume during OLV should be kept as high as in two-lung ventilation (*i.e.*, 8–10–12 ml/kg).

However, recent studies have shown that the lung injury after thoracotomy is also an important challenge in lung surgery, and the ventilatory setting (especially during OLV) is probably associated with this injury. So, a revision of the classic guidelines has been necessary.<sup>4</sup> This article is indeed an important step in this revision after some *in*

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Emulsion is not indicated for use in pediatric intensive care unit sedation because the safety of this regimen has not been established.<sup>2</sup> In the unusual event that a patient is required to be sedated “off label” with propofol, as stated in our article,<sup>1</sup> we recommend that doses of propofol be kept as low as effectively possible and that patients be monitored for hypotension, metabolic acidosis, and arrhythmia.

We also agree with Drs. Wappler and Horn that the complete information and all relevant data from trial 0859IL-0068 that was referred to in the introductory paragraph of our article<sup>1</sup> should be submitted to a peer-reviewed journal to help promote a better understanding of the association between propofol and the increased mortality that occurred in the propofol arms of the study.

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*vitro*<sup>5</sup> and *in vivo*<sup>6</sup> studies. However, in contrast to the current study, in the study of Schilling *et al.*,<sup>6</sup> decreased tidal volumes were associated with a (statistically insignificant) decrease in Pao<sub>2</sub> levels during OLV. This contrast may be a result of the fact that there was no positive end-expiratory pressure (PEEP) application in the control group in the current study. In several studies, it has been shown that PEEP was associated with an increase in oxygenation compared with zero end-expiratory pressure without any other change in ventilatory setting.<sup>7</sup> So, PEEP should be considered as a prevention/treatment strategy both against hypoxemia and against lung injury. Furthermore, information about and comparison of the number of the patients in each group in whom the fraction of inspired oxygen has been increased to treat arterial hypoxemia would also be necessary.

Therefore, I agree with authors that a protective ventilation (lower tidal volumes and PEEP) during OLV can lead to a decrease in lung injury during OLV; however, to argue that this method is also associated with improved oxygenation, a further study comparing low and high tidal volumes (with PEEP in both groups) would be necessary.

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**In Reply:**—I read with a great interest the comments formed by Dr. Şentürk about our article.<sup>1</sup> As suggested by Dr. Şentürk, the occurrence of lung injury represents undoubtedly a second major of concern in association with the induced hypoxemia after thoracotomy and one-lung ventilation. Regarding one-lung ventilation-related hypoxemia, the approach retaining the same tidal volume ( $V_T$ ) as during two-lung ventilation was due to pulmonary derecruitment with lower  $V_T$ <sup>2</sup> and overinflation after the adjunction of positive end-expiratory pressure (PEEP).<sup>3</sup> In accord with recent studies,<sup>4,5</sup> I believe that a protective ventilatory strategy during one-lung ventilation (reduced  $V_T$  and moderate level of PEEP) could prevent overinflation (and related lung injury) and preserve alveolar recruitment in settings characterized by reduced lung volume (*i.e.*, one-lung ventilation). Dr. Şentürk questions the interest of performing a further study comparing low *versus* high  $V_T$  with PEEP in both groups. In regard to this issue, the debatable point is not the influence of  $V_T$  alone but the interaction between PEEP and  $V_T$  with the determination of their optimal combination. Indeed, studies of acute lung injury have clearly demonstrated that respective effects are interdependent with a progressive derecruitment with reduced  $V_T$  counteracted by the adjunction of PEEP which ensures the best oxygenation.<sup>6,7</sup> Moreover, if the most important factor in the development of ventilator-induced lung injury is the end-inspiratory lung volume,<sup>8,9</sup> both high  $V_T$ <sup>10</sup> and a high level of PEEP<sup>11</sup> could be associated with oxygenation impairment related to a redistribution of pulmonary blood flow from overdilated lung units to the excluded lung or areas with low ventilation/perfusion ratio. Choi *et al.*<sup>4</sup> recently reported the lack of difference between reduced  $V_T$  (6 ml/kg) associated with a high level of PEEP (10 cm H<sub>2</sub>O) and a high level of  $V_T$  alone (no PEEP) on oxygenation. This contrasts with the results of our study previously published using a protective ventilation strategy with similar  $V_T$  (5 ml/kg) and lower PEEP level (5 cm H<sub>2</sub>O).<sup>1</sup> One can argue whether this last combination is close to the best between these settings.

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## Transient Neurological Dysfunction after Continuous Femoral Nerve Block: Should This Change Our Practice?

**To the Editor:**—We read with interest the report of Blumenthal *et al.*<sup>1</sup> of a case of prolonged neurologic deficits after regional anesthesia in a patient with an undiagnosed (subclinical) neuropathy. We congratulate

the authors on the exemplary treatment of the patient with a neurologic complication—early evaluation, appropriate investigations, and adequate support and follow-up till resolution.